Interleukin 7 receptor is required for myeloid cell homeostasis and reconstitution by hematopoietic stem cells.

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Public Summary:
Respiratory diseases are a leading cause of death worldwide, with vulnerability to disease varying greatly between individuals. The reasons underlying disease susceptibility are unknown, but there is often a variable immune response in lungs often. Recently, we identified a surprising novel role for the interleukin 7 receptor (IL7R), a primarily lymphoid-associated regulator, in fetal-specified, lung-resident macrophage development. Here, we report that traditional, hematopoietic stem cell-derived myeloid cells in the adult lung, peripheral blood, and bone marrow also depend on IL7R expression. Using single- and double-germline knockout models, we found that eosinophil numbers were reduced on deletion of IL7Ralpha. We then employed two Cre recombinase models in lineage tracing experiments to test whether these cells developed through an IL7Ralpha+ pathway. Despite the impact of IL7Ralpha deletion, IL7R-Cre labeled only a minimal fraction of eosinophils. We therefore examined the intrinsic versus extrinsic requirement for IL7R in the production of eosinophils using reciprocal hematopoietic stem cell transplantation assays. These assays revealed that extrinsic, but not eosinophil-intrinsic, IL7R is required for eosinophil reconstitution by HSCs in the adult lung. To determine which external factors may be influencing eosinophil development and survival, we performed a cytokine array analysis between wild-type and IL7Ralpha-deficient mice and found several differentially regulated proteins. These findings expand on our previous report that IL7R is required not only for proper lymphoid cell development and homeostasis, but also for myeloid cell homeostasis in tissues.

Scientific Abstract:
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